In re Application of
David Sidransky
U.S. Serial No.: 09/420,433
Filed: October 12, 1999
Exhibit A

PATENT
Attorney Docket No.: JHU1180-1

EXHIBIT A

CLAIMS UPON ENTRY OF THE AMENDMENT

1. (Amended) A method for detecting the presence of a mammalian mutant target nucleic acid which contributes to the etiology of a neoplasm, in a tissue specimen, wherein the specimen is external to a primary neoplasm and the specimen does not exhibit morphological characteristics indicative of neoplastic pathology, and the mutant target nucleic acid is present in the primary neoplasm and the specimen, the specimen being selected from the group consisting of a tumor margin and a regional lymph node, the method comprising extracting nucleic acid present in the specimen and detecting the presence of the mutant target nucleic acid.

2. (Amended) The method of claim 1, further comprising amplifying the nucleic acid present in the specimen to produce an amplified nucleic acid before detecting the presence of the mutant target nucleic acid in the amplified nucleic acid.

3. (Amended) The method of claim 2, wherein said amplifying is by means of oligonucleotides that hybridize to flanking regions of the mutant target nucleic acid.

4. (Amended) The method of claim 1, wherein the mutant target nucleic acid contains a mutation selected from the group consisting of a restriction fragment length polymorphism, a nucleic acid deletion, and a nucleic acid substitution.

5. (Amended) The method of claim 1, wherein the mutant target nucleic acid is selected from the group consisting of an oncogene and a tumor suppressor gene.

6. (Amended) The method of claim 1, wherein the mutant target nucleic acid is a tumor suppressor gene selected from the group consisting of APC, DCC, NF1, NF2, Rb, RET, VHL, WT-1 and p53.

7. (Amended) The method of claim 1, wherein the neoplasm is a neoplasm of the head.

8. (Amended) The method of claim 1, wherein the neoplasm is a neoplasm of the neck.

9. (Amended) The method of claim 1, wherein the neoplasm is a benign neoplasm.

10. (Amended) The method of claim 1, wherein the neoplasm is a malignant neoplasm.

11. (Amended) The method of claim 2, further comprising cloning the amplified nucleic acid before detecting the presence of the mutant target nucleic acid in the amplified nucleic acid.

12. (Amended) A method for detecting metastases in a subject having an excised tumor, the method comprising:

a) isolating tissue from a surgical margin or lymph node adjacent to the excised tumor;

b) applying to said tissue an oligonucleotide that specifically hybridizes to a neoplastic nucleic acid having a mutant nucleotide sequence; and

c) detecting the presence of said neoplastic nucleic acid, wherein the presence of said neoplastic nucleic acid indicates metastases.

13. The method according to claim 12 wherein no more than an average of about one out of every ten thousand cells of said tissue have a neoplastic nucleic acid.

14. The method according to claim 12 wherein said tissue appears normal under a microscope.

15. The method according to claim 12 wherein said neoplastic nucleic acid is a mutated tumor suppressor gene.

16. The method according to claim 15 wherein said tumor suppressor gene is the *p53* gene.

17. (Amended) The method according to claim 12 wherein said neoplastic nucleic acid is an oncogene.

18. (Amended) A method for detecting a mammalian target neoplastic nucleic acid having a mutant nucleotide sequence in a tissue specimen which is external to a primary neoplasm, comprising extracting nucleic acid present in the specimen to obtain extracted nucleic acid, and detecting the presence of the target neoplastic nucleic acid in the extracted nucleic acid.

EXHIBIT B

Webster's II

New College Dictionary

Houghton Mifflin Company
Boston • New York